

# Experimental Investigation of Hypoplastic Left Heart Syndrome (HLHS)

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## INTRODUCTION

Hypoplastic Left Heart Syndrome (HLHS) is a rare but serious congenital heart defect in which the left ventricle fails to develop fully. Several treatments are available to correct the malformation, but they are highly invasive with mixed success rates. Despite a successful correction, quality of life is significantly reduced and life expectancy is only half that of the general population. Without treatment, the condition is fatal<sup>[1]</sup>. Both genetic and environmental factors are believed to cause HLHS<sup>[1]</sup>. One factor attributed to the development of HLHS is the failure to maintain normal flow through the heart in the fetus<sup>[2]</sup>. *In vivo* experiments on zebrafish embryos have demonstrated that a similar condition can be produced by obstructing flow through the developing heart by the insertion of a bead<sup>[4]</sup>. Altered ventricular wall shear stresses resulting from the occlusion were attributed as the cause of the abnormal development. To better understand the fundamental fluid dynamics involved in HLHS, we have undertaken an *in vitro* study involving the design and construction of a left heart model to allow for detailed, quantitative measurements of flow patterns and wall shear stresses in the developing heart, with a longer-term goal of quantifying the effects of occlusions on wall shear stresses.

## METHODOLOGY

### Left Heart Construction

To understand the flow phenomena in the left heart, a quasi-two-dimensional rigid model was designed, as shown in Figure 1. While the model does not adequately replicate many three-dimensional features or the time-varying geometry of the human heart, it provides (a) a simplified system for the testing and validation of experimental methods, (b) a highly-controlled environment where boundary conditions can be replicated in concurrent numerical simulations, and (c) a simpler platform for the investigation of salient flow features. The heart model was designed using Pro Engineer® and the negative was molded via rapid prototyping. The atrium and ventricle were modeled based on a semi-elliptical cross-section. A 2-D bi-leaflet valve was used in place of the actual 3-D tri-leaflet valve, which could not be replicated in a 3-D model. Multiple iterations of valves were tested. The final valve was made of .00075" polyester shim stock. The box was constructed using 7/16" acrylic plates enclosing dimensions 3"X3.81"X5". To prevent leakage, the final heart had 4 sides permanently cemented together with 2 removable section for model cleaning and valve exchange. Chordae tendinae and papillary muscles were not modeled. Pulsatile fluid flow was regulated using a DC motor driven piston pump controlled using *National Instruments* LabVIEW software and an electronic motor controller.

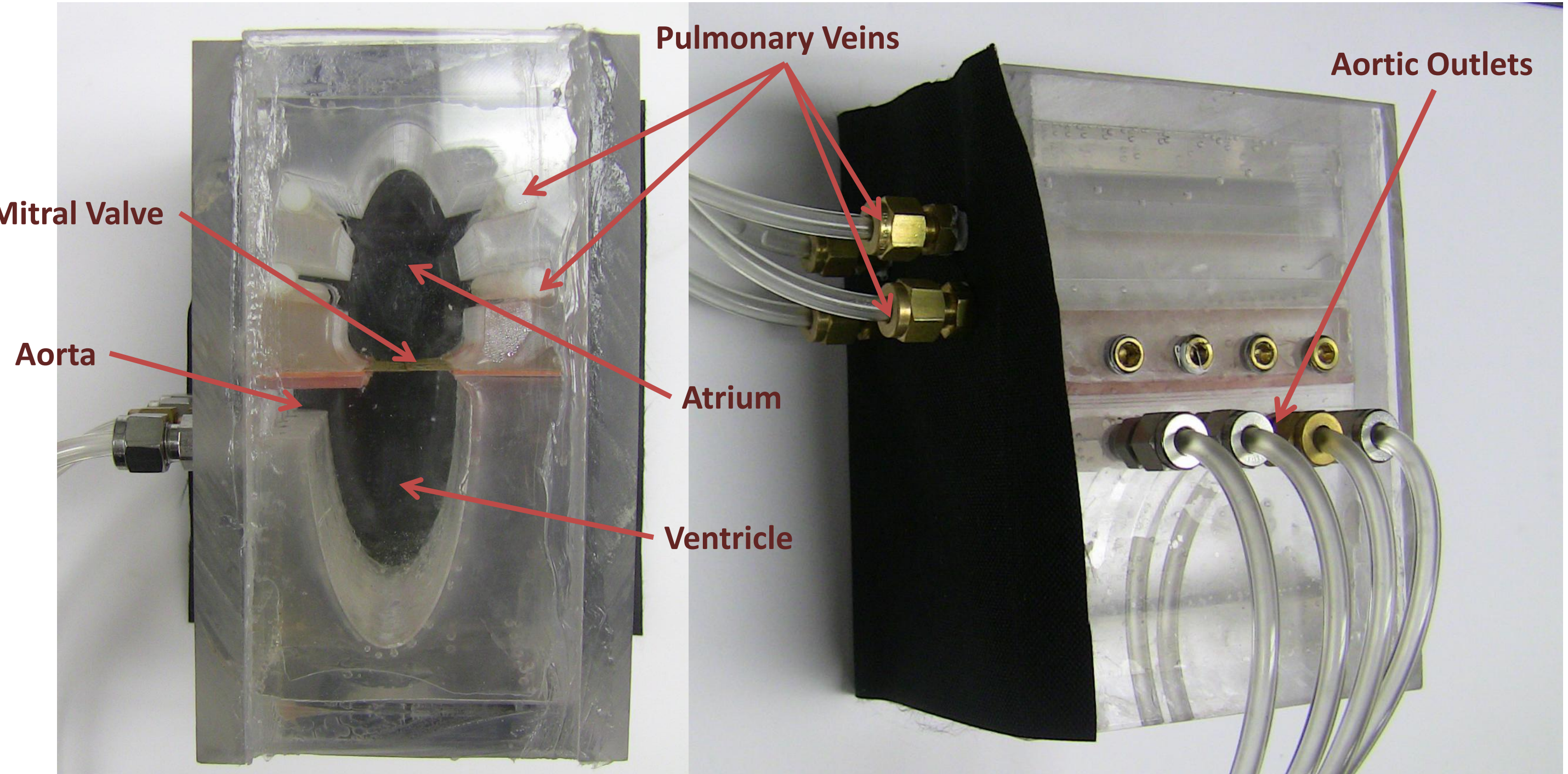


Figure 1 : Final Heart Model (left) and Initial Test Model (right)

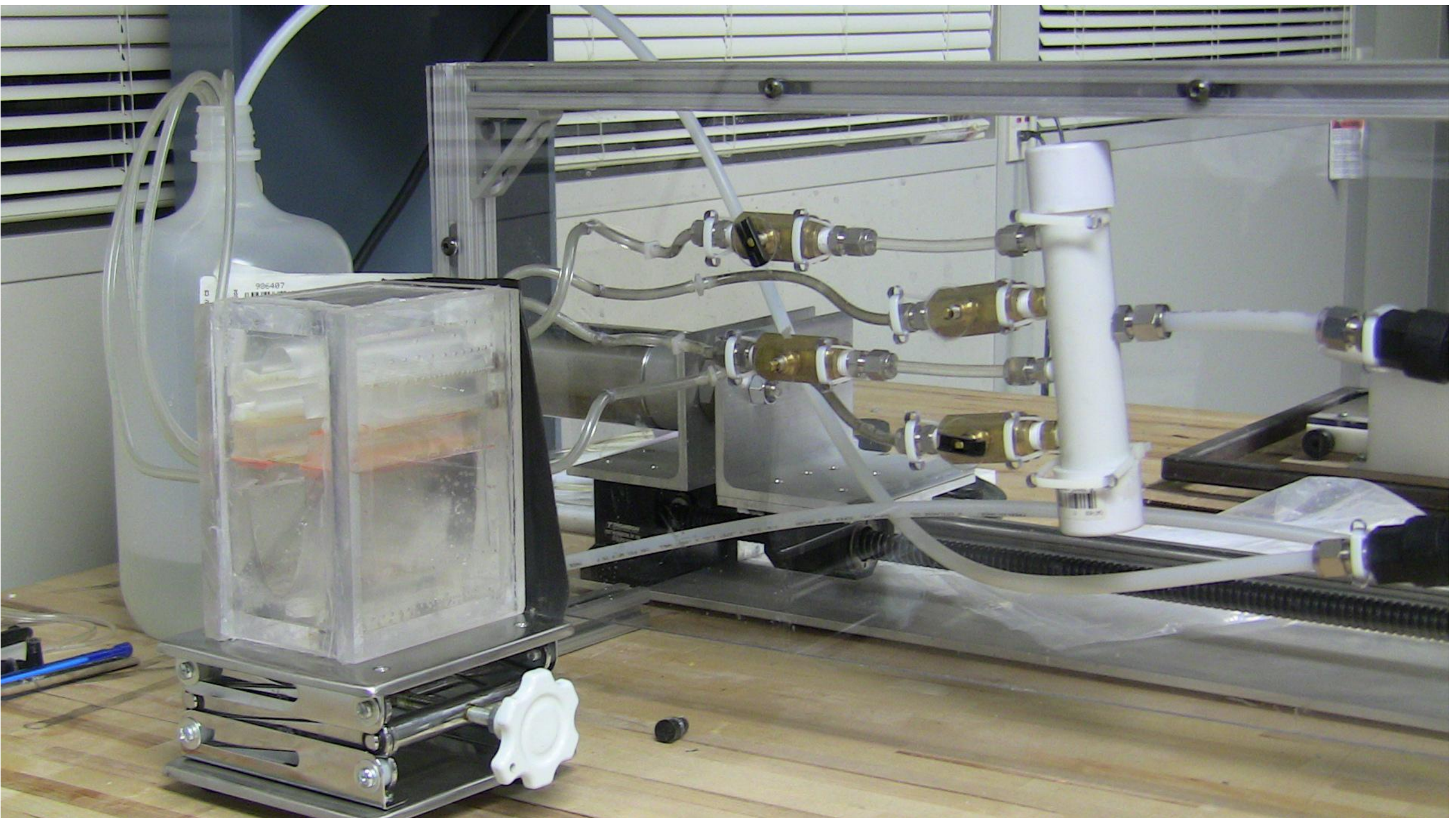


Figure 2. Final Left Heart Model and Pump Assembly

The pump displaces 178 mL of water, 70% of the model's ventricular volume, in a given cycle. Water was used as the working fluid. Four pulmonary inlet tubes ran the length of the pulmonary veins. Polyester filter media was packed into each vein to evenly disperse the fluid entering the left atrium in an effort to create a two-dimensional flow field. Four aortic outlets were utilized in the final model to minimize back pressure and its related fluid effects.

### Digital Particle Image Velocimetry (DPIV)

DPIV<sup>[4,5,6]</sup> was used to measure the velocity field in the left heart model. In this method, the flow is seeded with micron-sized particles that are illuminated using two spatially-coincident pulsed laser sheets separated by a known time interval. The laser sheets are located at the symmetry plane of the model as shown in Figure 3. A CCD camera captures images of the two laser-illuminated particle distributions, and a cross-correlation analysis within corresponding sub-windows of two images yields a local average displacement. Combining the displacement with the known time interval between the images yields a local velocity vector. Resulting two-dimensional vector fields in the heart model are shown in Figure 4. Such vector fields can be used to examine flow patterns and flow-induced ventricular wall stresses.

### Dimensionless Parameters

The Reynolds number ( $Re$ ), a measure of dynamical scale, and Womersley number ( $\alpha$ ), reflecting the degree of unsteadiness in the flow, are the primary parameters governing fluid flow in this model. Both parameters, defined below, are based on the mitral valve diameter ( $d$ ) and time-averaged velocity through the mitral valve  $U$  over one cycle. The other variables are the kinematic viscosity  $\nu$ , and the heartbeat frequency  $f$ . Based on estimated flow rates and measurements of the dimensions of a 106-day fetal lamb heart by Dr. Randy Stevens (Drexel University), the model was designed for  $Re \approx 600$  and  $\alpha \approx 10$ .

$$Re = \frac{Ud}{\nu}$$

$$\alpha = \frac{d}{2} \left( \frac{2\pi f}{\nu} \right)^{\frac{1}{2}}$$

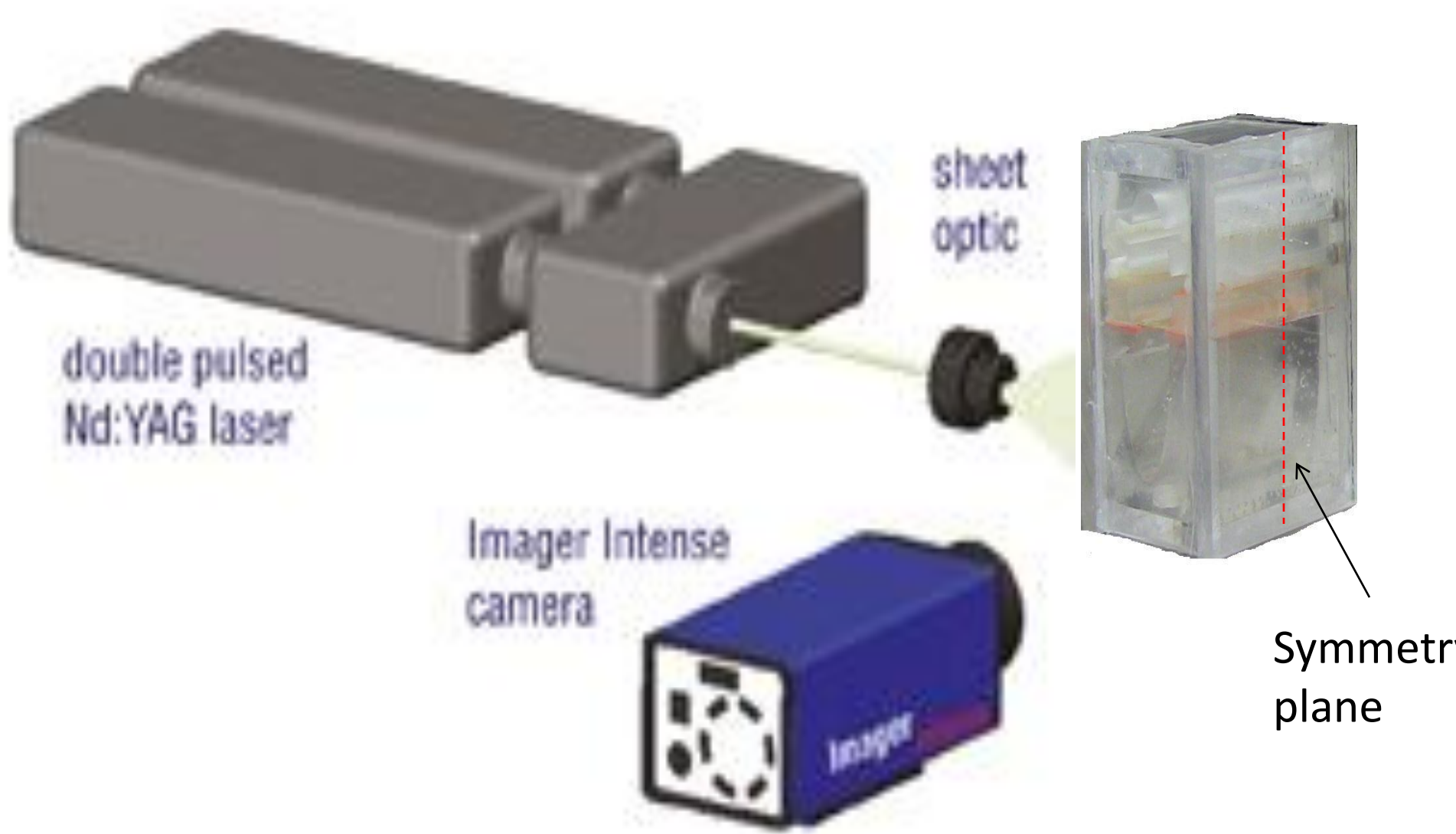


Figure 3: DPIV setup

## RESULTS

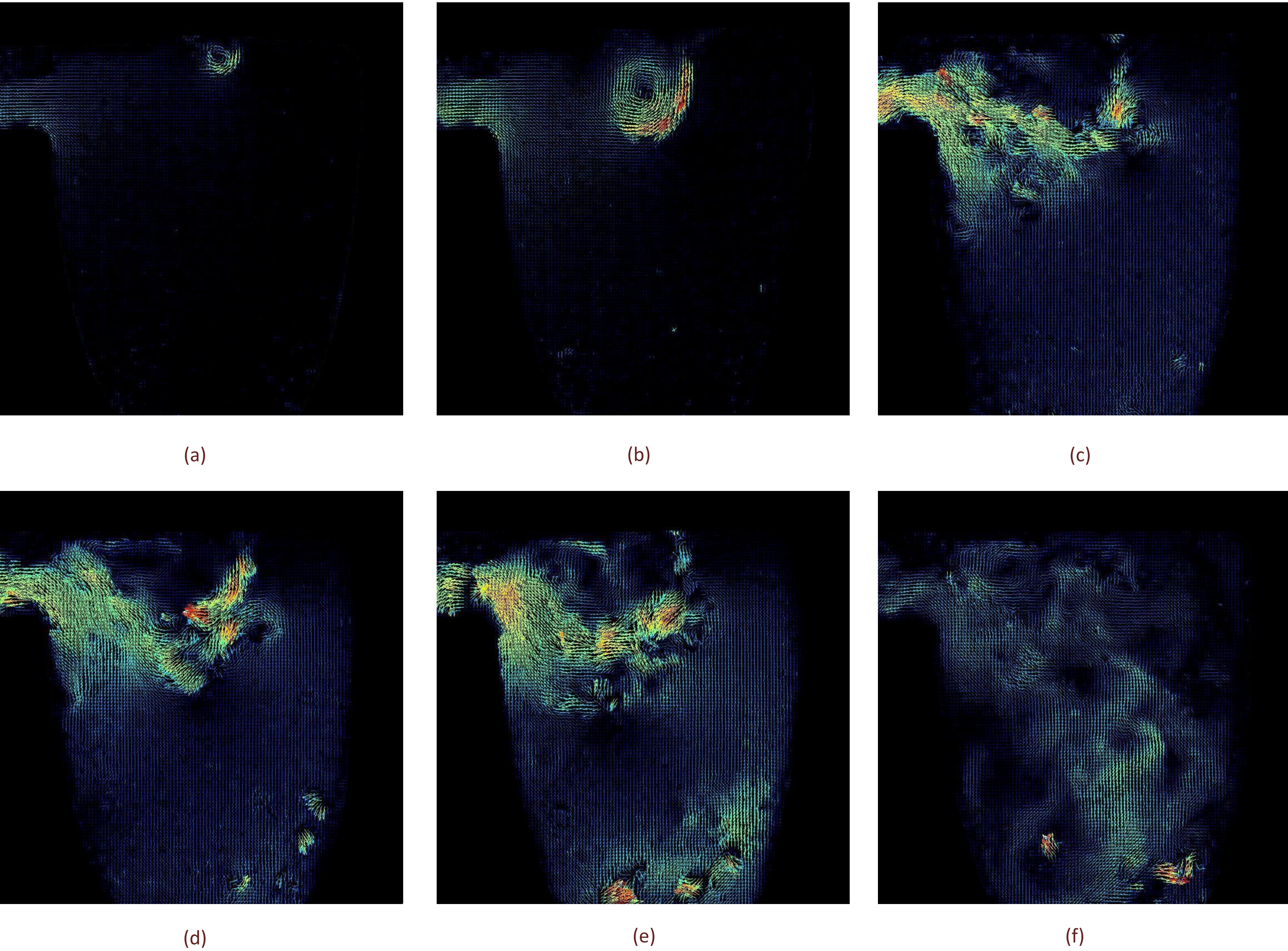


Figure 4. Flow evolution in the symmetry plane of the left ventricle. Velocity magnitude is indicated by arrow length and color.

Figure 4 contains vector plots illustrating the evolution of the flow field in the symmetry plane of the heart model over the course of one heartbeat. Because the ventricle walls are rigid, flow must enter the atrium and exit through the aorta simultaneously (Figure 4a). This results in asymmetric vortex formation through the mitral valve (Figure 4b). In comparison, the *in-vivo* pattern shown in Figure 5 reveals the formation of a counter-rotating vortex pair below the mitral valve, which is known to be a robust feature of left ventricular flow.

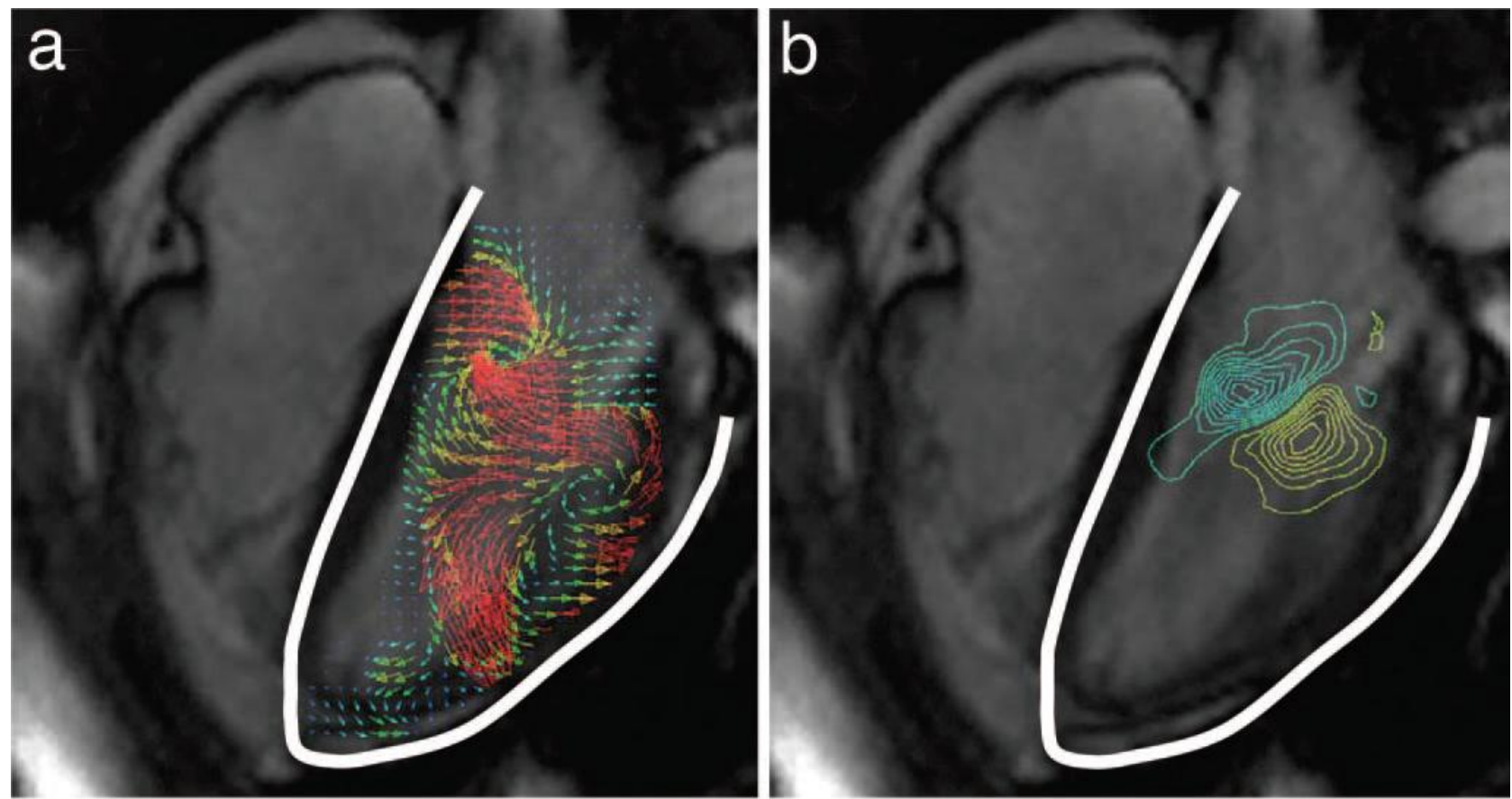


Figure 5: (a) velocity and (b) vorticity fields measured *in vivo*<sup>[3]</sup>. Note in Figure 5b, the vortical flow mapped within a human heart. Green denotes clockwise rotation while yellow denotes counter-clockwise rotation just off the tips of the mitral valve.

A further deviation from expected flow behavior is seen in Figure 4c, where a lateral jet-like flow is formed. Flow introduced through the mitral valve is immediately drawn out through the aorta preventing its penetration deeper into the ventricle. Eventually (Figures 4 d-f), significant velocities develop near the bottom of the ventricle. This is an indication that a two-dimensional flow field has not been achieved – faster moving fluid from in front of or behind the measurement plane is being drawn into the measurement plane.

## DISCUSSION & CONCLUSIONS

A two-dimensional, rigid-walled left heart model was designed and built, including a flexible symmetric bi-leaflet mitral valve. DPIV was successfully applied to measure the velocity field in the symmetry plane of the model, which illustrated that the resulting flow patterns deviated significantly from those found *in vivo*. Furthermore, the flow field was not highly two-dimensional. The model has been useful for preliminary testing of our flow diagnostic methodologies and it is expected that it will serve as a useful test bed for further refinement of DPIV to measure wall shear stress. However, since the flow field shown in Figure 4 did not capture salient flow features reported from *in vivo* measurements, it is not likely useful to understand the fluid dynamic factors contributing to HLHS.

Currently, a three dimensional model is being explored. The ViVitro Left Heart System from ViVitro Labs Inc. ([www.vivitolabs.com](http://www.vivitolabs.com)) is currently being employed to better model the dynamics of a real human heart. The system, shown in Figure 6 contains a deformable clear silicon ventricular wall and can accommodate a variety of prosthetic mitral valves. Adjustments to aortic root and peripheral circulatory compliance and resistance can also be made to accurately emulate the interaction of the left ventricle with the rest of the circulatory system. We plan to implement DPIV in this system to characterize the flow field as we have done here, and to subsequently investigate the effect of occlusions introduced into the atrium on ventricular flow patterns and wall shear stresses.

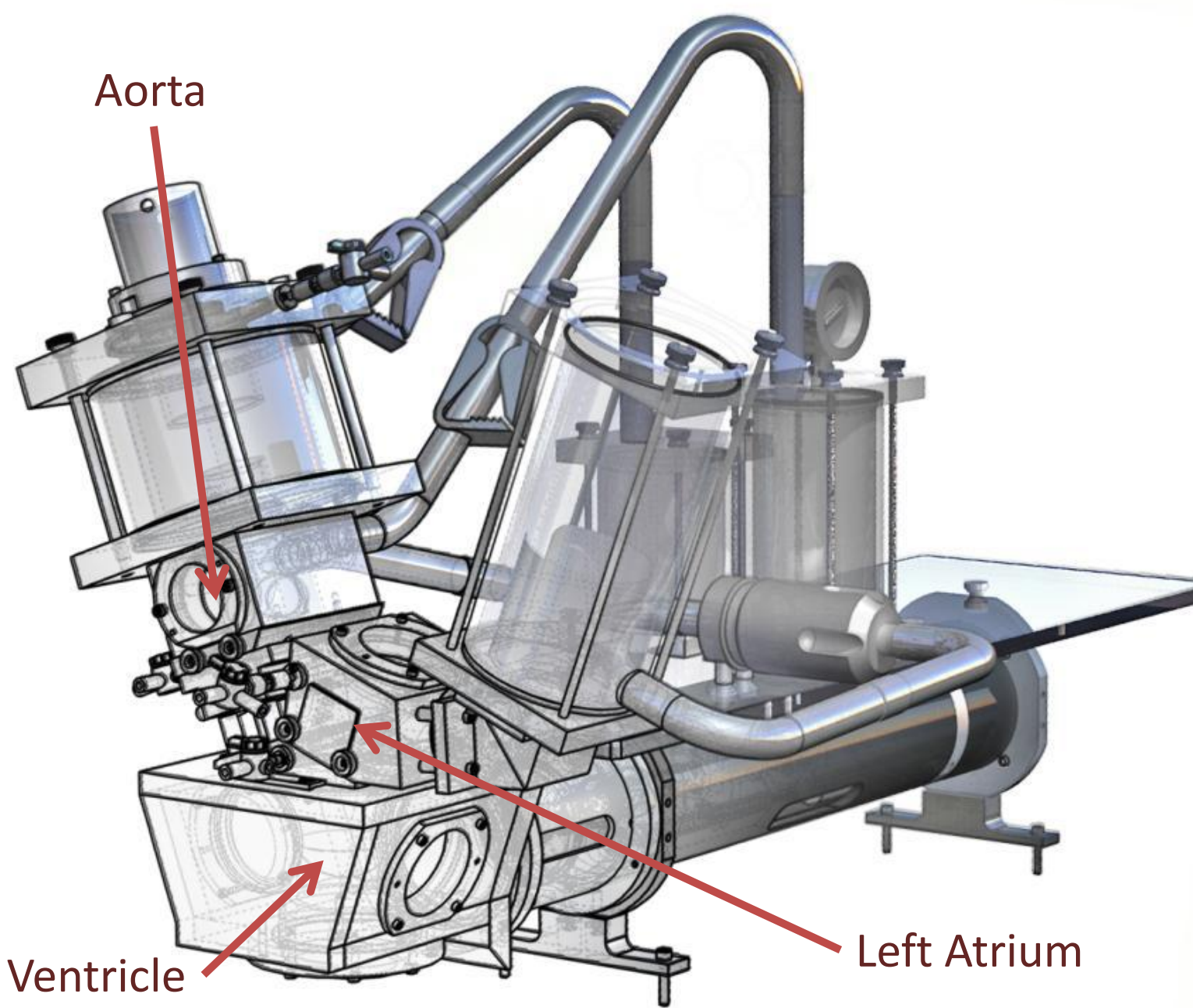


Figure 6. ViVitro Labs Model Left Heart System

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